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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,677	10/17/2003	John Guy	5853-324	9515

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
11/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,677	GUY, JOHN	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-25* is/are pending in the application.

4a) Of the above claim(s) *19-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/07/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 10/08/2007 has been entered. Claim 2 was cancelled. Claims 1, and 3-25 are pending. No claim was amended.

Claims 19-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, and 3-18 are currently under examination.

This application 10/687,677 filed on October 17, 2003 claims the benefit of 60/419,435 filed on 10/18/2002.

Claims 1, and 3-18 are currently under examination.

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 08, 2007 has been entered.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 3, and 8-16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Guy (Guy, Gene therapy for nuclear complementation of the G11778A LHON mitochondrial DNA mutation, Neurology, (April 24, 2001) Vol. 56, No. 8 Supplement 3, pp. A14. print. Meeting Info.: 53rd Annual Meeting of the American Academy of Neurology. Philadelphia, PA, USA. May 05-11, 2001. American Academy of Neurology. CODEN: NEURAI. ISSN: 0028-3878). Previous rejection is ***maintained*** for the reasons of record advanced on pages 7-8 of the office action mailed on 12/18/06.

Applicant's Arguments

Applicants have attached the 37 C.F: R. § 1.131 Declaration by Dr. John Guy. As per the declaration, the inventor had conceived the invention around 1997 and diligently proceeded towards reducing the invention to practice during the period from March 2000 through the filing of US Provisional Patent Applications: 60/271,073, filed February 23, 2001; US Provisional Patent Application 60/275,288, filed March 12, 2001; and, U.S. Patent Application No. 10/164,363 on June 6, 2002. As such, the instant invention antedates the Guy (Guy, Gene therapy for nuclear complementation of the G11778A LHON mitochondrial DNA mutation, Neurology, (April 24, 2001) Vol. 56, No. 8 Supplement 3, pp. A14. print. Meeting Info.: 53rd Annual Meeting of the American Academy of Neurology. Philadelphia, PA, USA. May 05-11, 2001. American Academy of Neurology. CODEN: NEURAI. ISSN: 0028-3878) references as

Applicants conceived and reduced to practice the instant invention prior to the publication date of the cited reference.

Response to Applicant's Arguments

The declaration filed on 10/8/2007 by Dr. John Guy under 37 CFR 1.131 has been considered but is ineffective to overcome the Guy, 2001 reference.

It is noted that US provisional applications 60/271,073, 60/275,288, and U.S. Patent Application No. 10/164,363 are cited both in Applicant's arguments as well as in the 37 C.F: R. § 1.131 Declaration by Dr. John Guy (#8, page 4 of the Declaration)

With regard to US Provisional Patent Application 60/275,288, filed March 12, 2001, the Applicant of Provisional Application 60/275,288 is Michael D. Potter (filed on 03/13/2001, which is inconsistent with the information Applicant indicated) and the title of the Application is "Micro-electro-mechanical varactor and a method of making thereof". It is totally unclear to the Examiner why Applicant cited the Provisional Application 60/275,288 because the subject matter of 60/275,288 fails to relate to the subject matter, reducing cellular dysfunction caused by mitochondrial gene mutations, of instant application.

With regard to US Provisional Patent Application: 60/271,073, filed February 23, 2001, the Applicant of Provisional Application 60/271,073 is Kai Y. Xu (filed on 12/17/2001, which is inconsistent with the information Applicant indicated) and the title of the Application is "Peptide and antibody useful for increasing cardiac contractility". It is totally unclear to the Examiner why Applicant cited the Provisional Application 60/271,073 because the subject matter of 60/271,073 fails to relate to the subject matter, reducing cellular dysfunction caused by mitochondrial gene mutations, of instant application.

With regard to U.S. Patent Application No. 10/164,363 filed on June 6, 2002, the US Application U.S. Patent Application No. 10/164,363 is Kai Y. Xu (filed on 06/06/2002, which is consistent with the information Applicant indicated) and the title of the Application is "Inotropic effects of antibodies on cardiac contraction". It is totally unclear to the Examiner why Applicant cited U.S. Patent Application No. 10/164,363.

The Examiner also notes that the search of databases of US Patents and Patent Applications by the inventor Dr. John Guy only reveals instant application 10/687,677. Applicant is advised to clarify why Provisional Applications (60/271,073 and 60/275,288) and U.S. Patent Application No. 10/164,363 are cited and what is the connection, if any, between these three Applications and instant application (10/687,677).

Furthermore, it is noted that the statue of 102(b) rejection is as follows: A person shall be entitled to a patent unless - (b) *the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.* Therefore, the 37 C.F: R. § 1.131 Declaration filed by Dr. John Guy (the inventor of instant application) has no bearing as far as 102(b) rejection is concerned because the inventor had fully disclosed the instant invention in a scientific meeting by a meeting abstract (a printed publication) one year prior to the claimed priority date of instant application, 10/18/2002. A copy of the meeting abstract is provided below in this office action (Guy, Gene therapy for nuclear complementation of the G11778A LHON mitochondrial DNA mutation, Neurology, (April 24, 2001) Vol. 56, No. 8 Supplement 3, pp. A14. print. Meeting Info.: 53rd Annual Meeting of the American Academy of Neurology.

Philadelphia, PA, USA. May 05-11, 2001. American Academy of Neurology. CODEN: NEURAI. ISSN: 0028-3878).

OBJECTIVE: To recode a full length mitochondrial sequence (ND4) in the universal genetic code and deliver the recoded ND4 gene to cybrid cells containing the G11778A point mutation in mitochondrial DNA of Leber Hereditary Optic Neuropathy (LHON). Successful import of the wild-type ND4 subunit may reduce the degree of heteroplasmy of mutant to wild-type protein within the mitochondria, thus favoring a more normal functioning of the OXPHOS system and perhaps reducing the risk of visual loss in patients harboring this mtDNA mutation.

BACKGROUND: Unlike, mtDNA-encoded proteins, nuclear-encoded proteins that are synthesized within the cytoplasm are more hydrophilic, thus amenable to import into mitochondria by a cleavable mitochondrial targeting presequence. While targeting of less hydrophobic proteins back into mitochondria is not hard to achieve, mitochondrial encoded proteins are extremely hydrophobic and are difficult to import.

DESIGN/METHODS: The feasibility of complementing a mutation in the mitochondrial subunit ND4 (G11778A) was tested by construction of a nuclear encoded version of wild-type ND4. Codons read in a non-canonical fashion by the mitochondrial genetic system, such as the UGA codon that directs the insertion of tryptophan in mitochondria, but is a stop codon in the cytoplasm were converted to the universal genetic code. The coding sequence for a mitochondrial targeting peptide was appended to the reading frame and nuclear promoter and polyadenylation sequences were provided. Cybrid cells derived from patients with LHON were transfected by calcium phosphate precipitation with the fusion gene containing the mitochondrial targeting sequence linked to nuclear encoded ND4 and a short sequence encoding the Flag protein. Mitochondrial import of the fusion ND4-Flag protein was detected by immunofluorescence with a murine anti-flag antibody 2 days after transfection. Mitochondria were identified by a rabbit polyclonal antibody against SOD2 or by Mitotracker. To determine whether cybrids can be used as a model system to detect an improvement in OXPHOS by the gene transfer, the rate of ATP synthesis using complex 1 substrates (malate and pyruvate) was measured in the cybrids and compared to a control cell line with normal mtDNA.

RESULTS: Anti-flag immunofluoresence revealed successful import of the ND4flag fusion protein into approximately 5–10% of the transfected G11178A cybrid cells. The rate of ATP synthesis in the cybrids was reduced 63% (12.6 mM ATP/minute/10^7 cells) relative to the control cell line (29.5 mM ATP/minute/10^7 cells).

CONCLUSIONS: Successful import of the recoded ND4 together with the reduction of OXPHOS in the cybrids sets the stage for future experiments to clone the ND4-flag fusion gene into recombinant adenoassociated virus to increase the population of tranduced cybrid cells, then determination whether the recoded ND4 improves OXPHOS in the transduced cells.

Guy disclosed the successful import of ND4flag fusion protein into 5-10% of the transfected G11178 cybrid cell and the rate of ATP synthesis in the transfected G11778A cybrids

was reduced 63% relative to the control cell line. Guy 2001 also disclosed that, "the feasibility of complementing a mutation in the mitochondrial subunit ND4 (G1178A) was tested by *construction* of a nuclear encoded version of wild-type ND4. Codon read in a non-canonical fashion by the mitochondrial genetic system, such as *the UGA codon that directs the insertion of tryptophan in mitochondria, but is a stop codon in the cytoplasm were converted to the universal genetic codon*" (See Design/Method Guy et al., 2001). It is noted that "*construction* of a nuclear encoded version of wild-type ND4" clearly reads on *isolated* nucleic acid encoding a functional ND4 as recited in claim 1, whereas the statement "Codons read in a non-canonical fashion by the mitochondrial genetic system, such as the UGA codon that directs the insertion of tryptophan in mitochondria, but is a stop codon in the cytoplasm were converted to the universal genetic codon" clearly reads on claim 7 of instant application.

With regard to an enhancer element and a polyA tail (claims 13 and 14 of instant applicant), Guy et al. 2001 teach nuclear promoter (which broadly reads on an enhancer element) and polyadenylation sequences (which reads on polyA tail) were provided to construct and express mitochondrial subunit ND4 (G11778A) (See lines 7-10, the Design/Methods paragraph, Guy et al., 2001).

Thus Guy clearly anticipates amended claims 1, 3, and 8-16 of instant application.

3. Previous rejection of claims 1, 3-6, and 8-18 under 35 U.S.C. 102(a) as being anticipated by Guy et al. (Guy et al., Rescue of a mitochondrial deficiency causing Leber Hereditary Optic Neuropathy. *Ann Neurol.* 52(5): 534-42, 2002, published online *October 11, 2002*), is ***withdrawn*** because Applicants filed the 37 C.F.R. § 1.131 Declaration by Dr. John Guy to

antedate their findings and show that Applicants conceived and reduced to practice the instant invention prior to the publication date of the cited reference.

The declaration filed on 10/8/2007 by Dr. John Guy under 37 CFR 1.131 is sufficient to overcome the Guy et al. *Ann Neurol.* 52(5): 534-42, 2002 reference.

Specifically, on page 2 of the Declaration by Dr. John Guy indicates that Exhibit A are copies of Dr. John Guy's laboratory notebooks date March 13, 2001 showing: (1) The completion of packaging of the nuclear encoded ND4 subunit with appended FLAG epitope into the viral vector after more than 1 year of work in constructing this approximately 1500 bases from overlapping 80 mer oligonucleotides; (2) Demonstration of ND4Flag expression by western immunobloting of homogenates from infected cells; (3) Immunofluorescent microscopy of mitochondrial localization of ND4FLAG fusion protein using MitoTracker Red in transfected cell culture.

4. Previous rejection of claims 1, 8, 10-12, 15-18 under 35 U.S.C. 102(a) as being anticipated by Guy et al. (Guy et al., Gene therapy with the ND4 subunit gene recoded in the universal genetic code reverses a mitochondrial deficiency causing Leber Hereditary Optic Neuropathy (LHON), Neurology, (April 9, 2002) Vol. 58, No. 7 Supplement 3, pp. A508. print. Meeting Info.: 54th Annual Meeting of the American Academy of Neurology. Denver, Colorado, USA. April 13-20, 2002. CODEN: NEURAI. ISSN: 0028-3878), is ***withdrawn*** because Applicants filed the 37 C.F.R. § 1.131 Declaration by Dr. John Guy to antedate their findings and show that Applicants conceived and reduced to practice the instant invention prior to the publication date of the cited reference.

The declaration filed on 10/8/2007 by Dr. John Guy under 37 CFR 1.131 is sufficient to overcome the Guy et al. 2002 reference, Meeting Info.: 54th Annual Meeting of the American Academy of Neurology.

Specifically, on page 2 of the Declaration by Dr. John Guy indicates that Exhibit A are copies of Dr. John Guy's laboratory notebooks date March 13, 2001 showing: (1) The completion of packaging of the nuclear encoded ND4 subunit with appended FLAG epitope into the viral vector after more than 1 year of work in constructing this approximately 1500 bases from overlapping 80 mer oligonueleotides; (2) Demonstration of ND4Flag expression by western immunobloting ofhomogenates from infected cells; (3) Immunofluorescent microscopy of mitochondrial localization of ND4FLAG fusion protein using MitoTracker Red in transfected cell culture.

5. Claims 1, 3-6, and 8-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Manfredi et al. (Manfredi et al., U.S. Patent Application Publication No: 2004/0072774, Publication date, April15, 2004, which claims benefits of provisional application No. 60/358,935, filed on Feb. 23, 2002). Previous rejection is ***maintained*** for the reasons of record advanced on pages 12-14 of the office action mailed on 12/18/06.

Applicant's Arguments

Applicants have attached the 37 C.F: R. § 1.131 Declaration by Dr. John Guy. As per the declaration, the inventor had conceived the invention around 1997 and diligently proceeded towards reducing the invention to practice during the period from March 2000 through the filing of US Provisional Patent Applications: 60/271,073, filed February 23, 2001; US Provisional

Patent Application 60/275,288, filed March 12, 2001; and, U.S. Patent Application No. 10/164,363 on June 6, 2002. As such, the instant invention antedates the Guy (Guy, Gene therapy for nuclear complementation of the G11778A LHON mitochondrial DNA mutation, Neurology, (April 24, 2001) Vol. 56, No. 8 Supplement 3, pp. A14. print. Meeting Info.: 53rd Annual Meeting of the American Academy of Neurology. Philadelphia, PA, USA. May 05-11, 2001. American Academy of Neurology. CODEN: NEURAI. ISSN: 0028-3878) references as Applicants conceived and reduced to practice the instant invention prior to the publication date of the cited reference.

Response to Applicant's Arguments

The declaration filed on 10/8/2007 by Dr. John Guy under 37 CFR 1.131 has been considered but is ineffective to overcome the Manfredi et al. reference (Manfredi et al., U.S. Patent Application Publication No: 2004/0072774, Publication date, April15, 2004, which claims benefits of provisional application No. 60/358,935, filed on Feb. 23, 2002).

The issues of lack of relevance of the US provisional applications 60/271,073, 60/275,288, and U.S. Patent Application No. 10/164,363 cited in Applicant's arguments and in the 37 C.F: R. § 1.131 Declaration by Dr. John Guy (#8, page 4 of the Declaration), have been discussed in the preceding section of the rejection of claims 1, 3, and 8-16 under 35 U.S.C. 102(b) as being anticipated by Guy (Guy, Gene therapy for nuclear complementation of the G11778A LHON mitochondrial DNA mutation, Neurology, (April 24, 2001) Vol. 56, No. 8 Supplement 3, pp. A14. print. Meeting Info.: 53rd Annual Meeting of the American Academy of Neurology. Philadelphia, PA, USA. May 05-11, 2001. American Academy of Neurology. CODEN: NEURAI. ISSN: 0028-3878).

It is noted that the provisional application No. 60/358,935 of Manfredi et al. (Manfredi et al., U.S. Patent Application Publication No: 2004/0072774, Publication date, April15, 2004) was filed on 02/23/2002 whereas the provisional application No. 60/419,435 of instant application was filed on 10/18/2002. Therefore, Manfredi et al. is qualified as an 102(e) prior art over the claims of instant application because a person shall be entitled to a patent unless - *(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent* ***by another*** *filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.*

Manfredi et al. teach methods for introducing functional peptides into organelles. Additionally, the invention by Manfredi et al. provides a method for correcting a phenotypic deficiency in a mammal that results from a mutation in the mammal's mitochondrial DNA (mtDNA). The invention by Manfredi et al. further provides a method for treating a mitochondrial disorder in a subject in need of treatment therefor. Also provided is an expression vector that is useful for introducing a functional peptide encoded by an mtDNA sequence into a mitochondrion. The invention by Manfredi et al. also provides eukaryotic cells transformed by expression vectors that are useful for introducing functional peptides into organelles. Finally, the invention by Manfredi et al. provides a pharmaceutical composition comprising a non-nuclear nucleic acid sequence encoding a peptide for introduction into an

organelle, a nucleic acid sequence encoding an organelle-targeting signal, and a pharmaceutically acceptable carrier (See abstract and paragraph [0014], Manfredi et al.).

With regard to an isolated nucleic acid comprising a nucleotide sequence encoding a functional ND4 mitochondrial protein wherein said sequence comprises at least one eodon substitution of a mitochondrial codon with a nuclear codon (claim 1 of instant application), Manfredi et al. teach an expression vector that is useful for introducing a functional peptide encoded by a mitochondrial DNA (mtDNA) sequence into a mitochondrion, comprising: (a) a nucleic acid sequence encoding ATPase 6 subunit of F_0F_1-ATP synthase or *ND4* subunit of complex I, wherein the nucleic acid sequence is compatible with the *universal genetic code* (which reads on nuclear codon recited in claim 1 of instant application); and (b) a nucleic acid sequence encoding a mitochondrial-targeting signal, wherein the mitochondrial-targeting signal is selected from the group consisting of the N-terminal region of human cytochrome c oxidase subunit VIII, the N-terminal region of the P1 isoform of subunit c of human ATP synthase, and the N-terminal region of the aldehyde dehydrogenase targeting sequence (See claim 75, Manfredi et al.).

With regard to the codon substitution being replaced of a mitochondrial codon with a nuclear codon in construction of a nuclear version of functional ND4 mitochondrial protein (claims 2-6 of instant application), Manfredi et al. teach (i) 11 "non-universal" codons in MTATP6 (Met=ATA or ATG; Trp=TGA) (See Fig. 1, Manfredi et al.), (ii) the genetic system of mitochondria differs from other known genetic systems because it deviates from the standard, or "universal", genetic code in several ways. In particular, the UGA codon, which generally means "stop", codes for tryptophan in mammalian mitochondria; the AUA codon,

which generally codes for isoleucine, codes for methionine in mammalian mitochondria; and the AGA codon, which generally codes for arginine, means "stop" in mammalian mitochondria. Accordingly, where a mitochondrial nucleic acid sequence is used in the method of the present invention, it may be necessary to first mutagenize the nucleic acid sequence to render it compatible with the universal genetic code. In such instances, a mutagenized mtDNA-specified polypeptide is appended to a mitochondrial-targeting signal, expressed from the nucleus, and transported back to the mitochondria under the guidance of the signal peptide (See paragraph [0049], Manfredi et al.), (iii) a nucleic acid sequence encoding ATPase 6 subunit of F_0F_1-ATP synthase or *ND4* subunit of complex I, wherein the nucleic acid sequence is compatible with the *universal genetic code* (See for instance, paragraph [0020] and claim 75, Manfredi et al.), (iv) construction of recorded ND4F and Adeno-Associated virus vectors (See example 7, Manfredi et al.), and (v) strategy for allotropic expression of ND4 and allotropic ND4 improves cybrid cell survival (See example 10, Manfredi et al.).

With regard to the components of an expression vector (claims 8-14 of instant application), Manfredi et al. teach preparation of constructs (See Example 1, Manfredi et al.).

With regard to a cell being a human cell located in the optic nerve of a human (claims 15-18 of instant application), Manfredi et al. teach stable and efficient expression of the fusion gene in cells, (See paragraph [0123], Manfredi et al.).

Thus Manfredi et al. clearly anticipates claims 1, 3-6, and 8-18 as amended of instant application.

Conclusion

6. No claim is allowed.

A sequence search of SEQ ID No: 1 recited in claim 7 of instant application finds the only perfect match of sequences of SEQ ID No: 1 is the disclosure of Applicant's instant application.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you

would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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